



# Seizures: They Come in All Shapes and Forms

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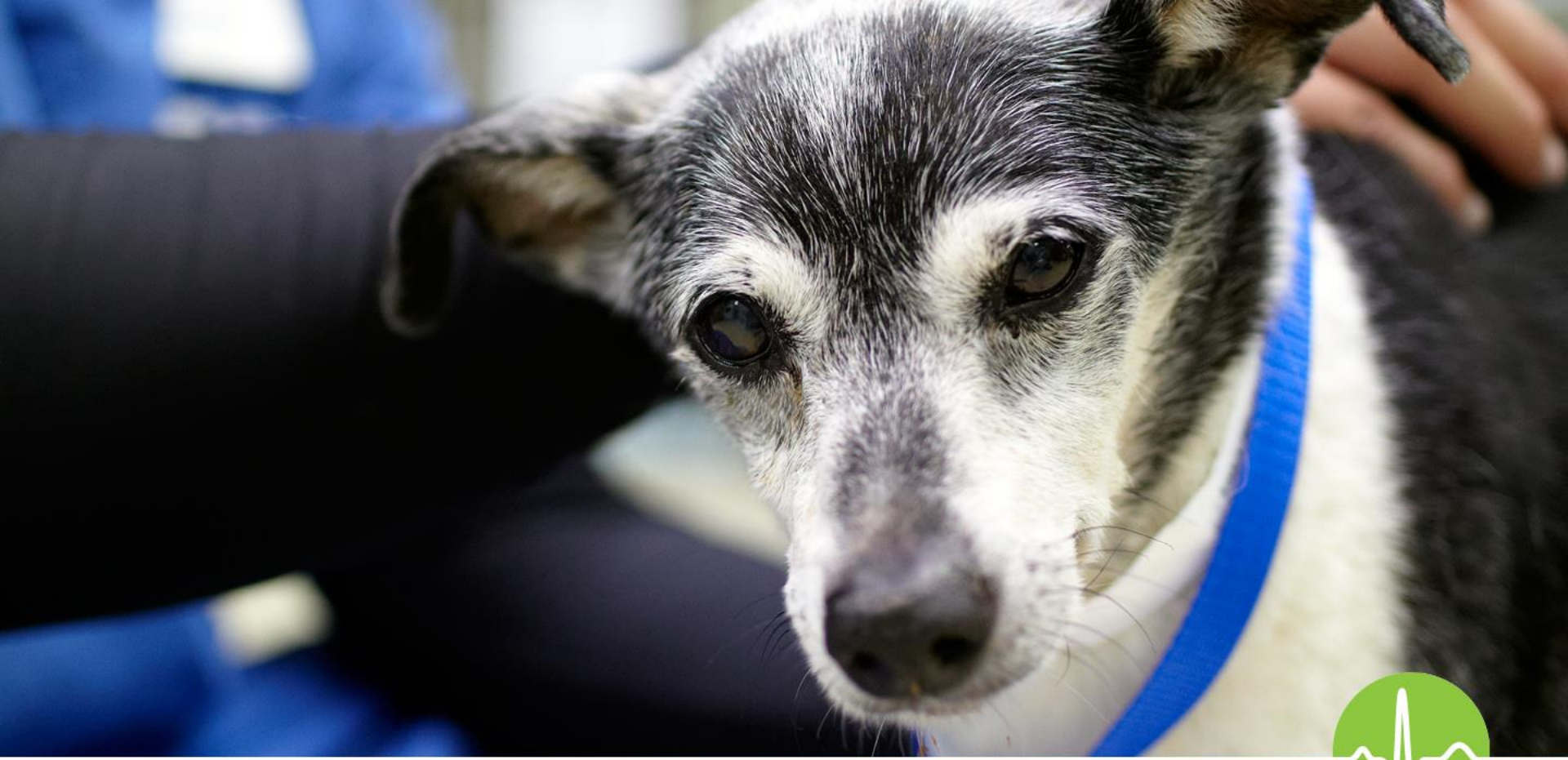


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# OVERVIEW

- Brief overview of seizure
- Minimum data base and work up for the seizure patient
- Review of real clinical cases





**Epilepsy “appears to me to be nowise more divine nor more sacred than other diseases...”**

Hippocrates

*On the Sacred Disease*



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# DIAGNOSTIC APPROACH TO EPILEPSY

- Pathogenesis
- Minimum data base
- Types of seizures
- Etiologic classification
  - Reactive
  - Symptomatic
  - Idiopathic

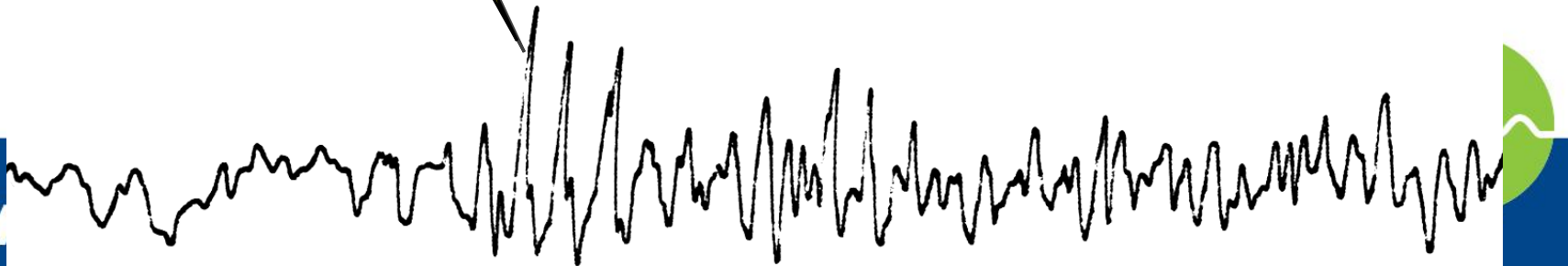
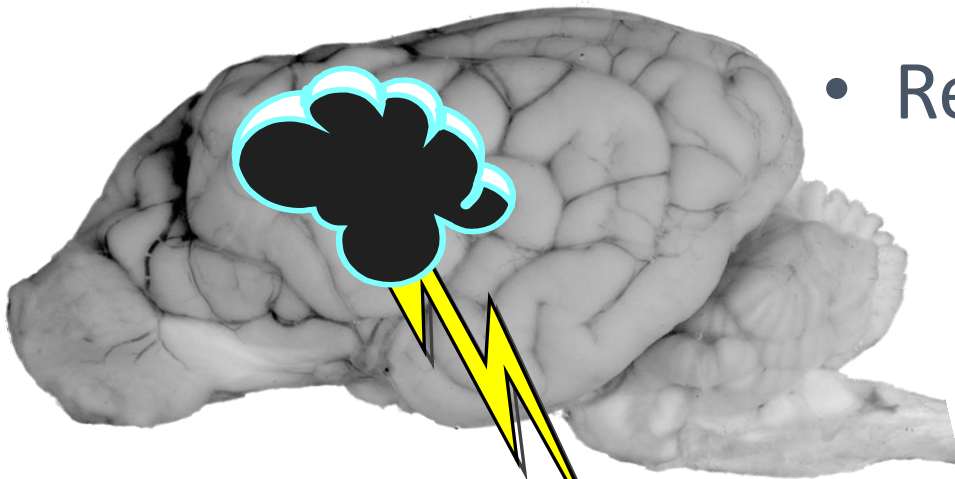




# ARISE FROM CEREBRAL CORTEX

## FOREBRAIN DISEASE

- Abnormal EEG
- Like seizures, come & go
- Rely on clinical signs



# CLINICAL SIGNS

- Loss or altered consciousness
- Altered tone or movement
- Autonomic disturbance
- Altered behavior  
(sensation)



# EPILEPSY

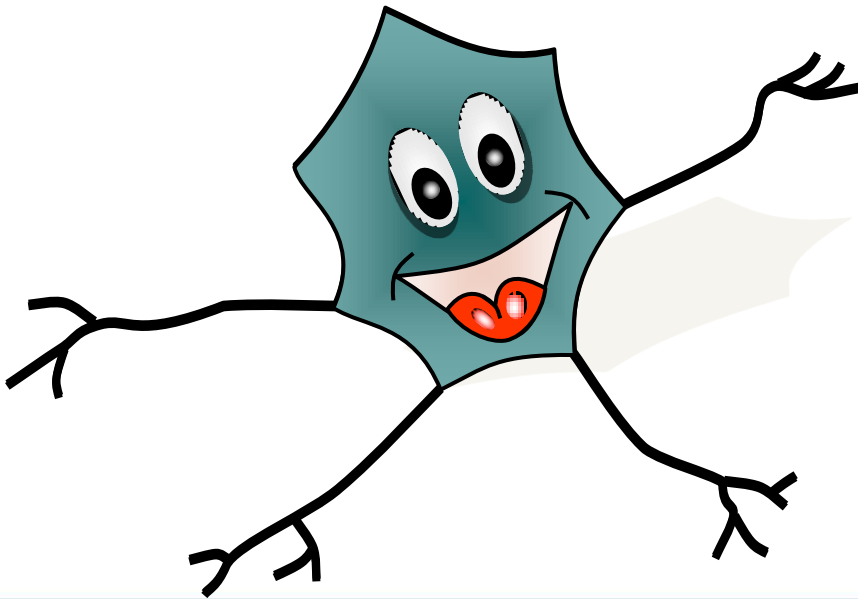
- Repeated seizures
  - Sign of cerebral disease
  - Many different causes

Sun	Mon	Tues	Wed	Thur	Fri	Sat
						
						
						



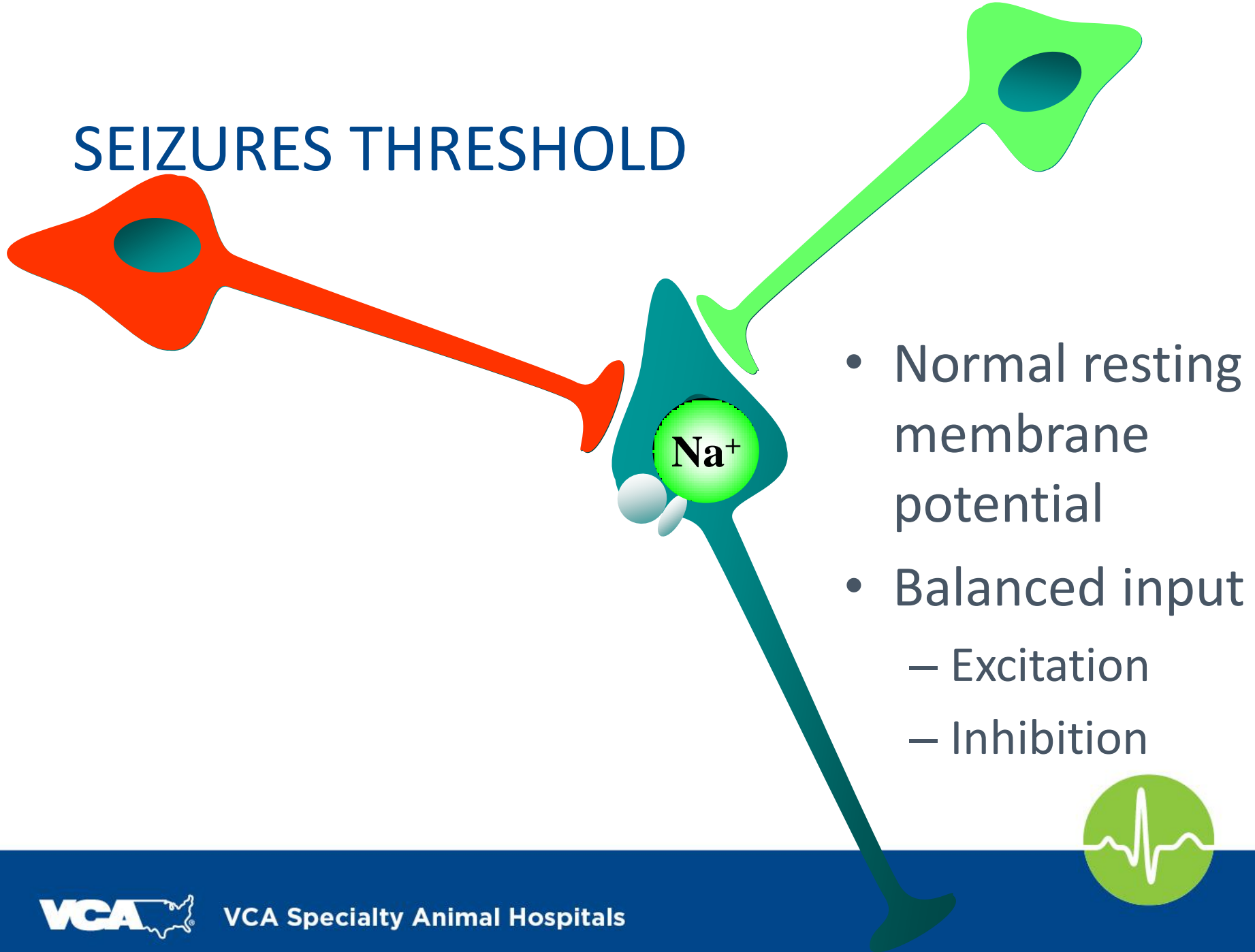
# SEIZURES

- Excess excitation
- Too many neurons firing synchronously





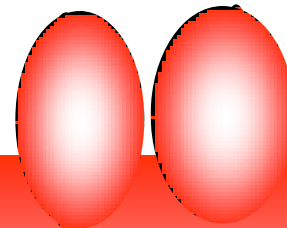
# SEIZURES THRESHOLD



# SEIZURE TERMINATION

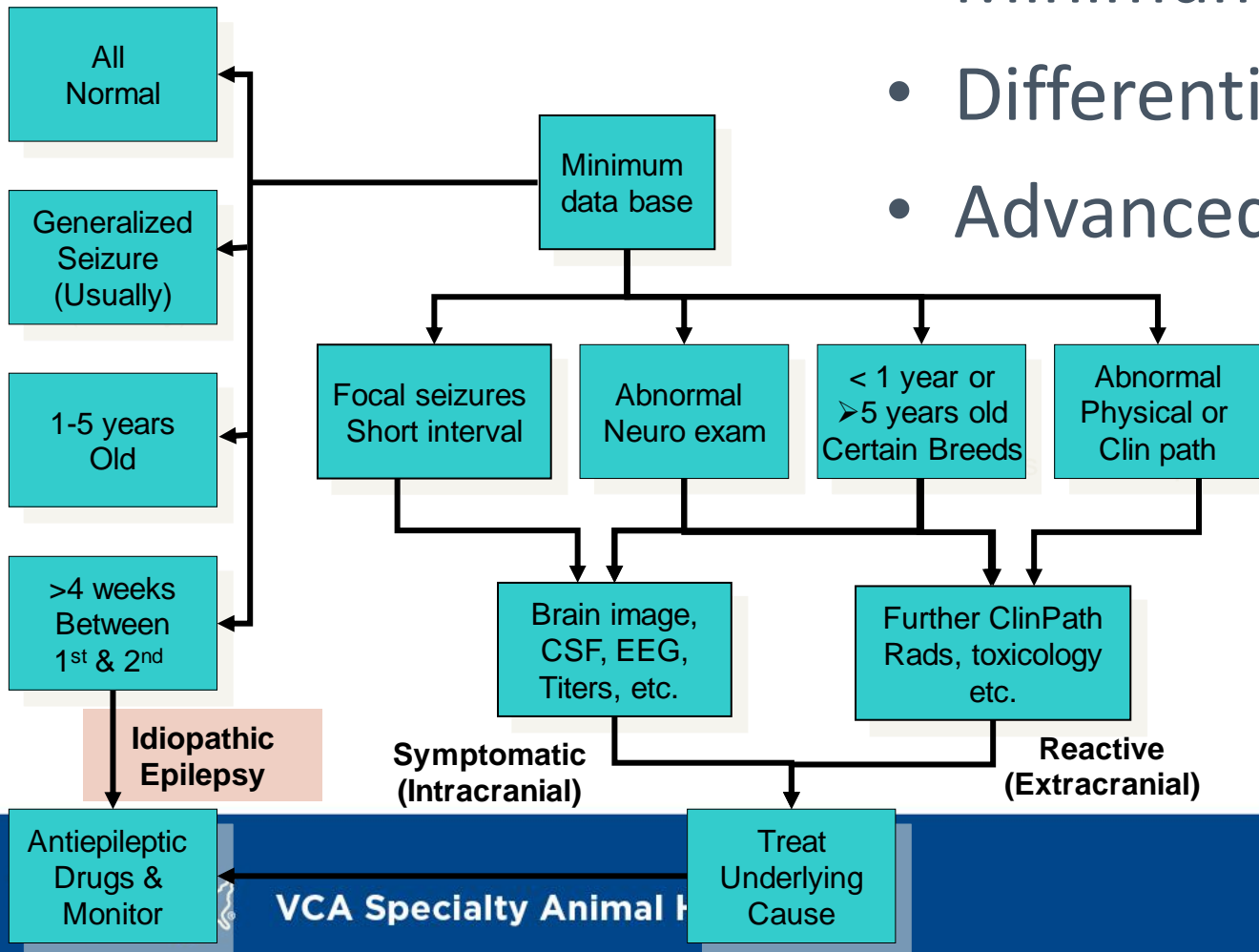


- Most < 2 minutes
- Terminated by  $K^+$  currents



# DIAGNOSTIC APPROACH

- Minimum data base
- Differential diagnosis
- Advanced diagnostics



# ETIOLOGIC CLASSIFICATION

- Reactive – extracranial
  - Toxin or metabolic
- Symptomatic – intracranial
  - Tumor or encephalitis
- Primary or idiopathic – no recognized cause
  - Genetic?



# MINIMUM DATA BASE

- Signalment
- History
- Physical exam
- Neurologic exam
- Laboratory data

Minimum  
data  
base



# ADDITIONAL DIAGNOSTICS

- CBC/Chemistry panel
- Serum bile acids
- Thyroid panel
- Met check
- Advanced imaging (MRI, CT scan)
- CSF analysis
- Infectious titers
- Metabolic Profile
- Etc.





# SIGNALMENT

1-5 years of age



- Idiopathic epilepsy
  - 65% of dogs this age
  - 35% **NOT** idiopathic
    - Podell et al 1995
- Age NOT predictor of positive MRI findings with seizures
  - Abnormal neuro exam was
    - Busch et al 2001
- Breed predilections
  - Toy breeds
  - Brachiocephalic



# < 1 YEAR OLD



- **Anomaly**
- **Metabolic**
  - Glucose , liver, electrolytes
- **Nutritional**
- **Infections**
  - Distemper, rabies, protozoal, rickettsial, fungal
- **Toxins**
  - Lead, pesticides, mycotoxins, plant
- **Trauma**



## > 5 YEARS OF AGE



- **D**egenerative
- **M**etabolic
- **N**eoplasia
- **N**utritional
- **I**nfarction
- **I**nfectious/immune
- **T**oxin
- **T**rauma



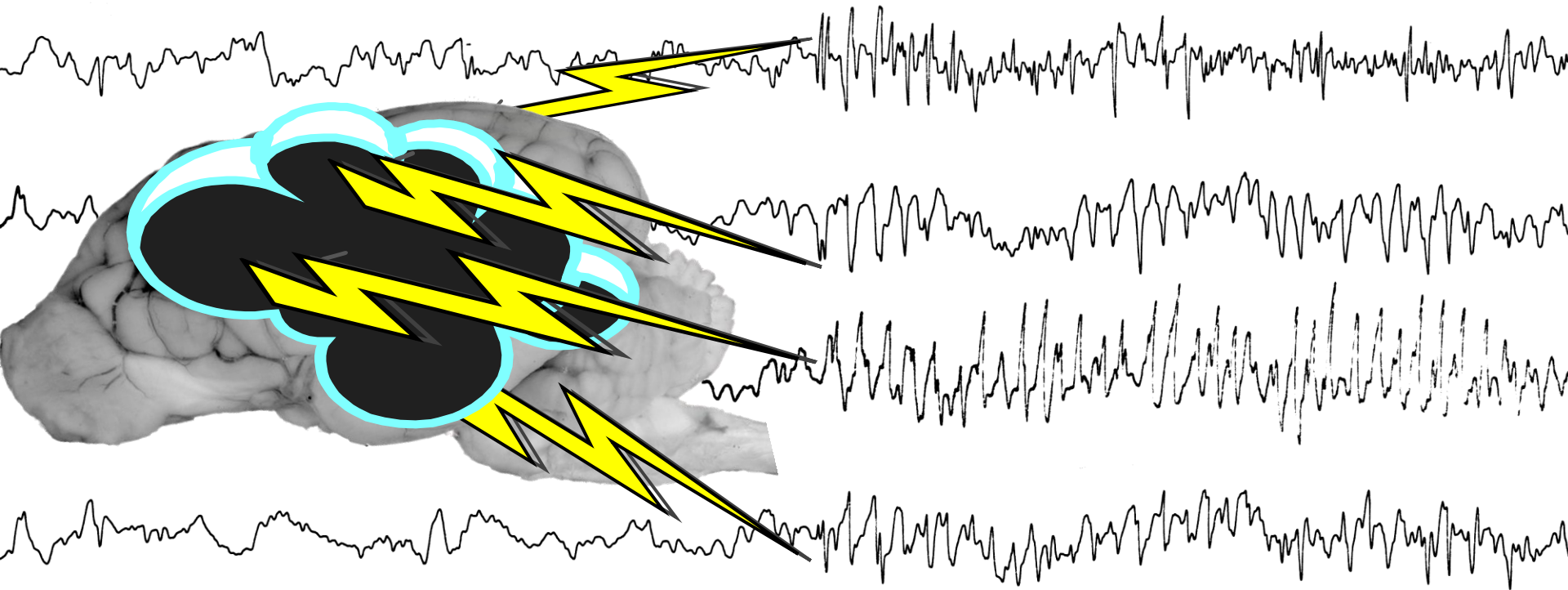
# TYPES OF SEIZURES

- Generalized
- Focal (partial)



# GENERALIZED SEIZURE

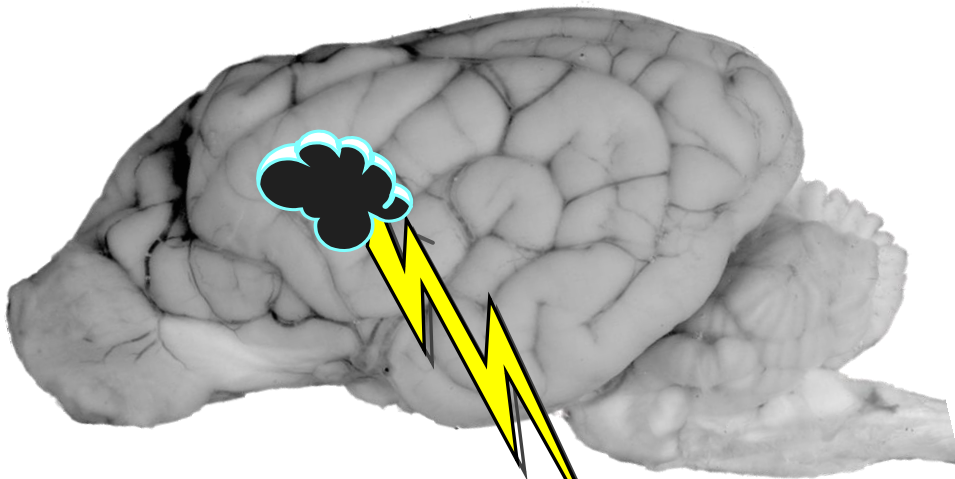
- Affects entire cortex at once





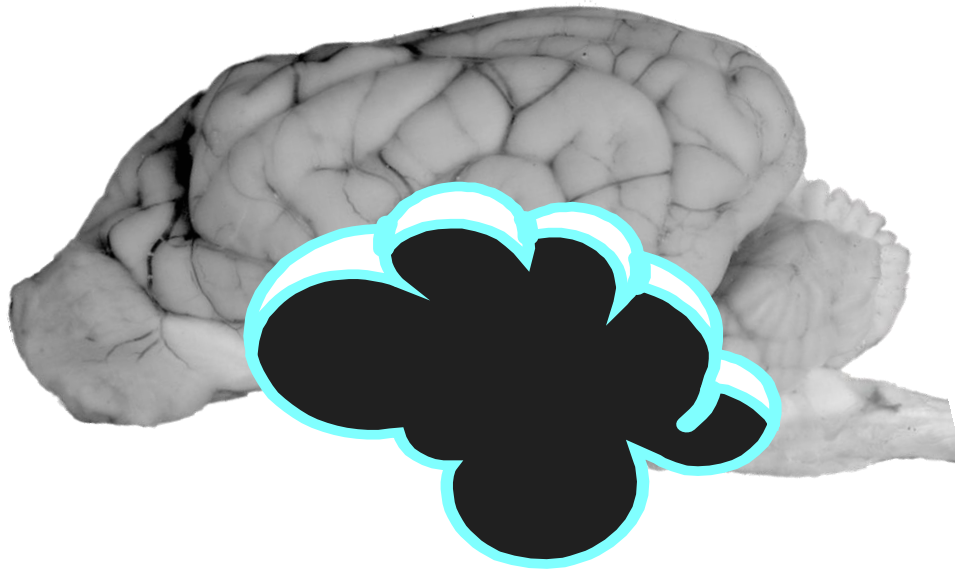
# FOCAL SEIZURE

- Storm starts in small area
- Signs depend on area

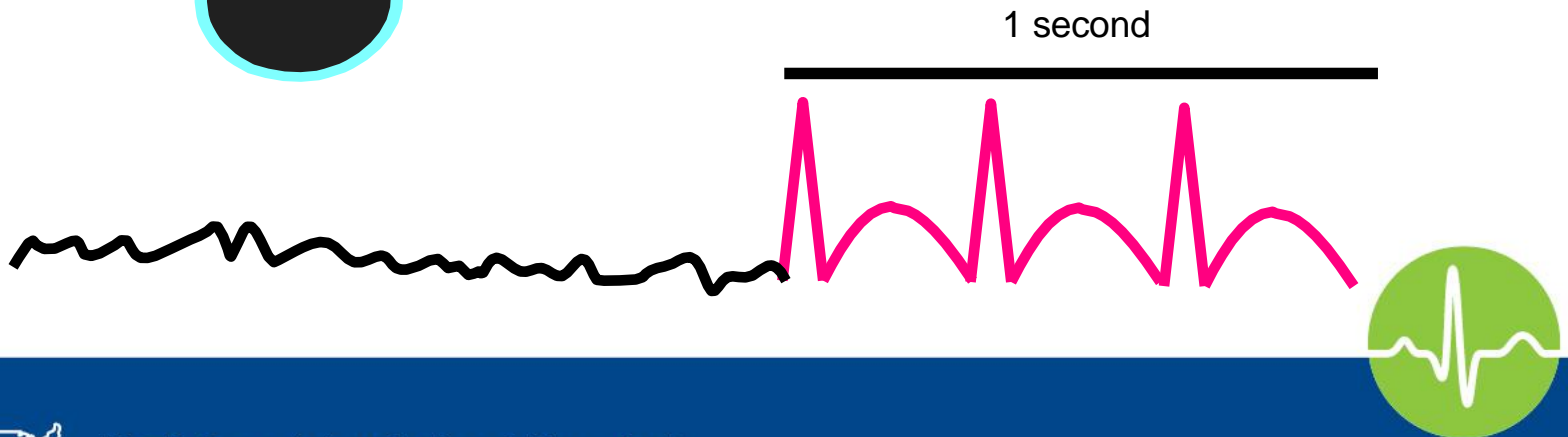




# PETIT MAL



- Generalized
  - Transient loss of contact with reality (Absence)
  - 3 Hz spike & wave
- Questionable in dog & cat
- Different drugs!!!!
- **Petit mal  $\neq$  Focal (partial)**



# CASE I



# CASE I



- 9 year old spayed female Labrador Retriever
- Patient has been having generalized seizure since 2 she was years old (presumptive idiopathic epilepsy)
- On AEDs (phenobarbital) since 3 years of age
- Seizures have been controlled well (2-3 seizures a year) up to 2-3 months ago
- Phenobarbital dose was increased and then started on KBr
  - Patient started having clusters and Keppra was added
- Continued to do poorly
- Blood work was unremarkable
- Patient presented for further evaluation and adjustment of AEDs

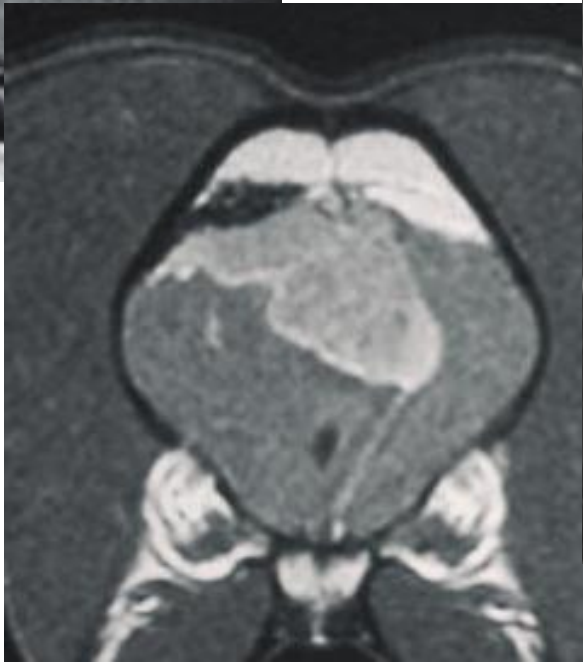
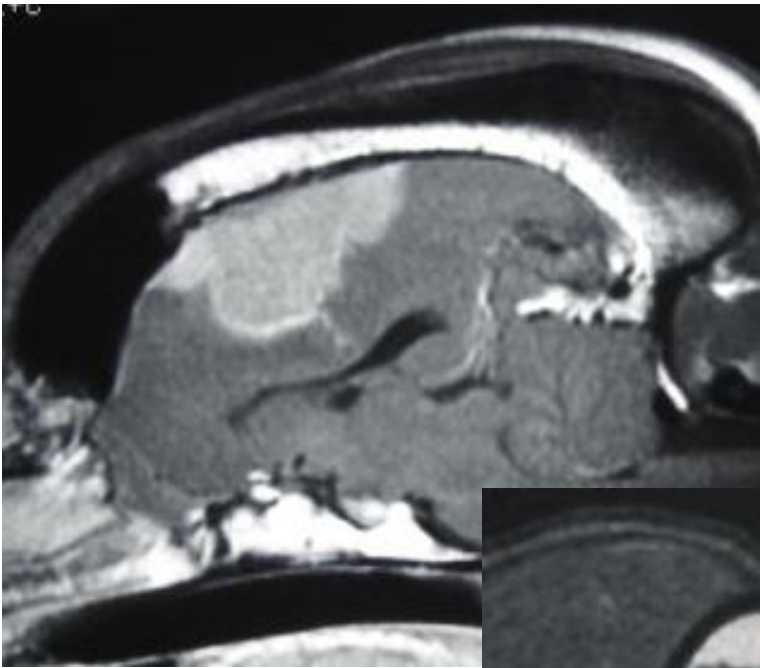


# CASE I



- Upon further questioning patient's behavior had altered recently; pacing consistently and appears “spacey”. Owner was under the impression the changes are from the AEDs.
- Neurological exam: inappropriate mentation, tendency to turn/circle to left, menace response deficits bilaterally (weaker OD), weak response to nasal stimulation on the right, fairly normal gait with postural reactions weaker in the right side
- Localization: Left prosencephalon





# CASE I



- Presumptive diagnosis: Meningioma
- Patient had surgery (craniotomy) followed by RT
- Histopathology: Psammomatous Meningioma
- Did well for over two years before return of the clinical signs and was euthanized at that time
- Lessons to be learned:
  - Patient's with history of idiopathic epilepsy could also get brain tumors as they become older
  - Correlate the clinical signs and presumptive diagnosis
  - Complete neurological exam is essential





# CANINE MENINGIOMA

- Extra-axial tumors
- 30%-49% of primary brain tumors
- Histologically benign w/ malignant biological behavior
- Grow under the dura mater
  - direct invasion of brain in ~ 27%
- Male:Female ratio = 0.6
- More common in dolicocephalic breeds
- Intracellular progesterone receptors
  - Inverse correlation between progesterone receptors and biological behavior
- Survival time
  - 2.5 – 30 months



Study	Therapy	Case #	Median survival time (mo)	Range
Foster et al	Corticosteroids	13	2.5	1 d – 13 mo
Platt et al	Corticosteroids	10	3.9	2.8 – 6 mo
Plat et al	RT + corticosteroids	28	7.4	6 – 20 mo
Spugnini et al	RT + corticosteroids	22	8.3	NR
Rossmeisl	Surgery	6	16.5	1.2 – 22.5 mo
Axlund et al	Surgery	16	7	0.5 – 22 mo
Niebauer et al	Surgery +/- RT or corticosteroids	10	7	NR
Platt et al	Surgery + RT + corticosteroids	22	14.9	12.6 – 20.5 mo
Axlund et al	Surgery + RT	11	18	3 – 58 mo
Theon et al	Surgery + RT	20	30	21 – 39 mo



## CASE II

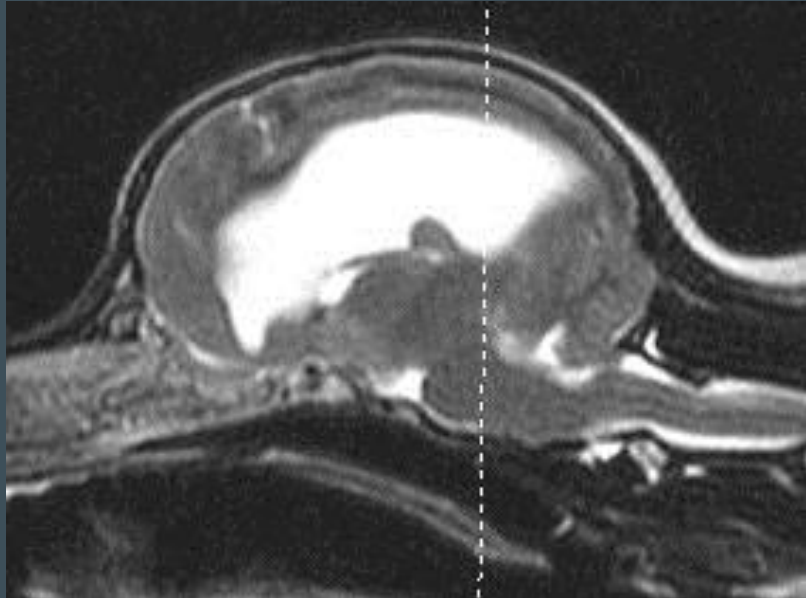


## CASE II



- 7 month old female spayed Bichon Frise
- Started having seizures about three months ago
- Normal blood work
- Patient was started on phenobarbital (2 mg/kg bid) and became very sedate, switched to Keppra after one week
- Seizures were controlled fairly well for six weeks but patient started declining neurologically (inappropriate mentation and bumping into objects)
- Patient was stuporous upon presenting to us



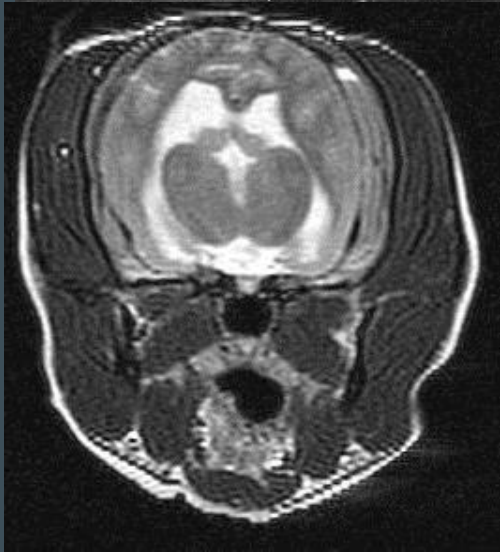
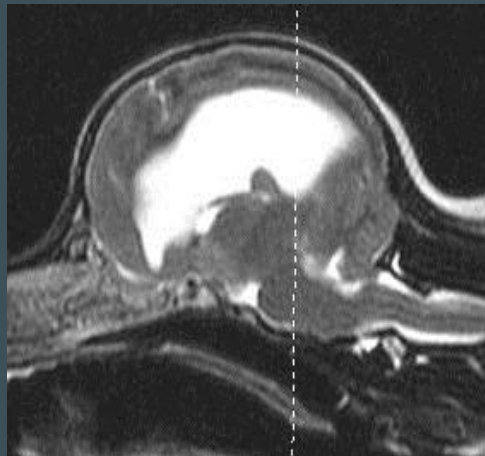
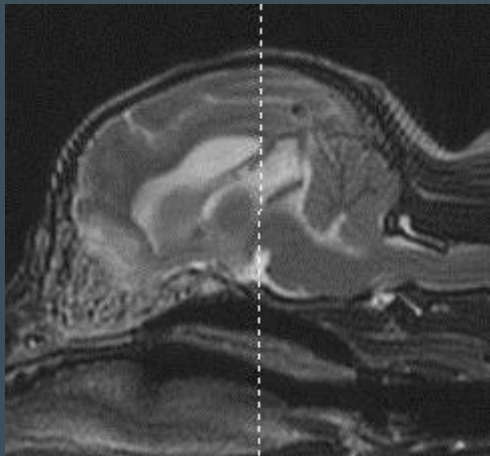




Post-op VP shunt placement







6 month post-op MRI

Pre-op MRI



# CASE III



## CASE III



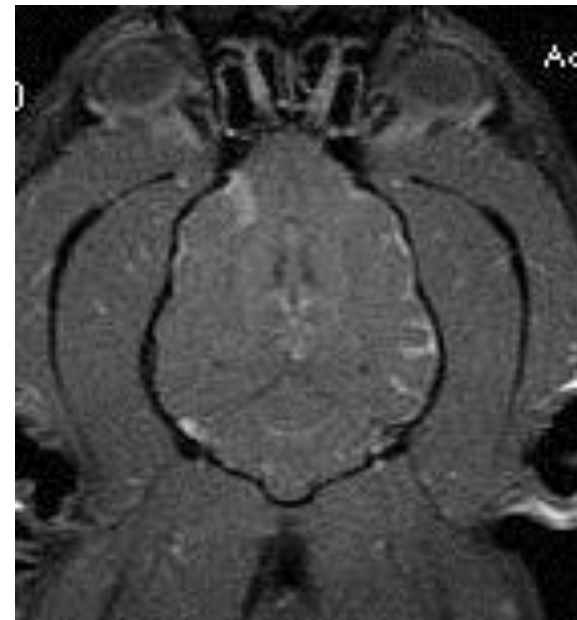
- Four year old female Labrador Retriever
- 3 month history of seizures and abnormal mentation
- Started on phenobarbital
- Clinical signs progressed into ataxia, dull mentation, and recent blindness
- Started on a short course of anti-inflammatory dose of prednisone about 4 weeks ago. Showed great response initially but signs relapsed and worsened after discontinuing the prednisone.
- Started on higher dose of prednisone for a presumptive GME. Showed response for couple of days and then declined.
- Upon presentation patient was non-ambulatory tetraparetic with obtunded mentation and absent menace response bilaterally.



## CASE III



- MRI of brain was highly suggestive of meningoencephalitis



Source:	CSF
Color	Colorless
Clarity	Clear
Specific Gravity	1.007
WBC	778 /uL
RBC	10 /uL



#### Cytology 1st Site

Cytology

#### CLINICAL INFORMATION:

##### SOURCE:

CSF; 1 cytospin sample available for evaluation.

#### DESCRIPTION/MICROSCOPIC FINDINGS/COMMENTS:

##### DESCRIPTION:

The numbers of nucleated cells appear markedly increased in a clear background with rare erythrocytes. A cellular differential reveals 90% eosinophils, 6% non-degenerate neutrophils, 1% large mononuclear cells, and 3% small mature lymphocytes. Several structures compatible with Cryptococcus are observed. These structures have a 5-15 micron spherical basophilic to magenta staining central structure surrounded by a large clear capsule. Narrow-based budding is observed. No evidence of neoplasia is appreciated.

#### MICROSCOPIC FINDINGS: CRYPTOCOCCOSIS WITH MARKED EOSINOPHILIC INFLAMMATION.

##### COMMENT:

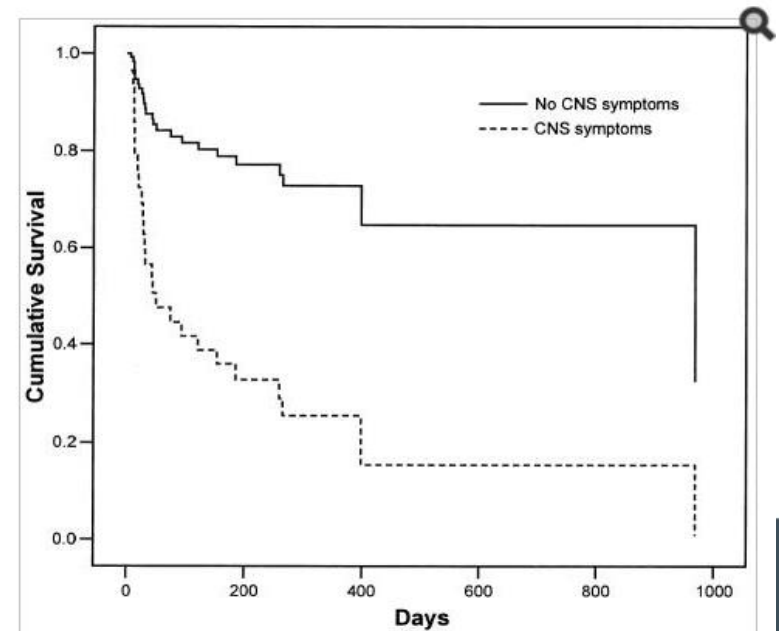
The findings indicate cryptococcal infection. A marked eosinophilic pleocytosis is noted in accompaniment.



## CASE III



- Diagnosed with cryptococcal meningoencephalitis
  - Treatment with antifungal and low dose steroid therapy was initiated
  - Patient was euthanized after few days of hospitalization
- *Cryptococcus neoformans*
  - Found worldwide
  - Infection thought to usually initiate in the lung. Disseminates to other sites, including CNS, skin, and eyes.





# VARIATIONS ON THE THEME

## GENERALIZED SEIZURES

- Clonic/tonic
- Pure tonic
- Pure clonic
- Myoclonic
- Atonic (drop attack)
- Etc.





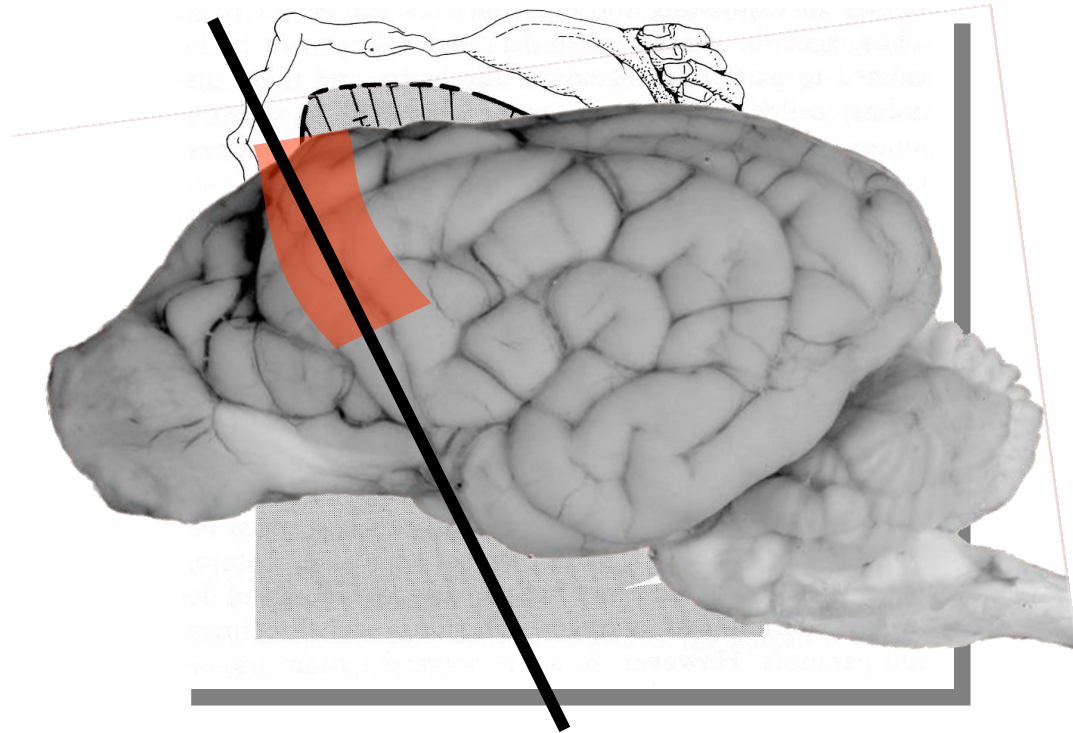
# VARIATIONS ON THE THEME



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# FOCAL MOTOR SEIZURES

- Starts in motor cortex
- Usually lateralized
- +/- altered consciousness



# FOCAL MOTOR SEIZURES



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# FOCAL MOTOR SEIZURES



# SEIZURES PRESENT IN MANY DIFFERENT WAYS!





## SEIZURES PRESENT IN MANY DIFFERENT WAYS!



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## SEIZURES PRESENT IN MANY DIFFERENT WAYS!



# SEIZURES PRESENT IN MANY DIFFERENT WAYS!



# SEIZURES PRESENT IN MANY DIFFERENT WAYS!



# FELINE EPILEPSY

- Few idiopathic



# GENERALIZED (GRAND MAL) SEIZURES



# GENERALIZED (GRAND MAL) SEIZURES

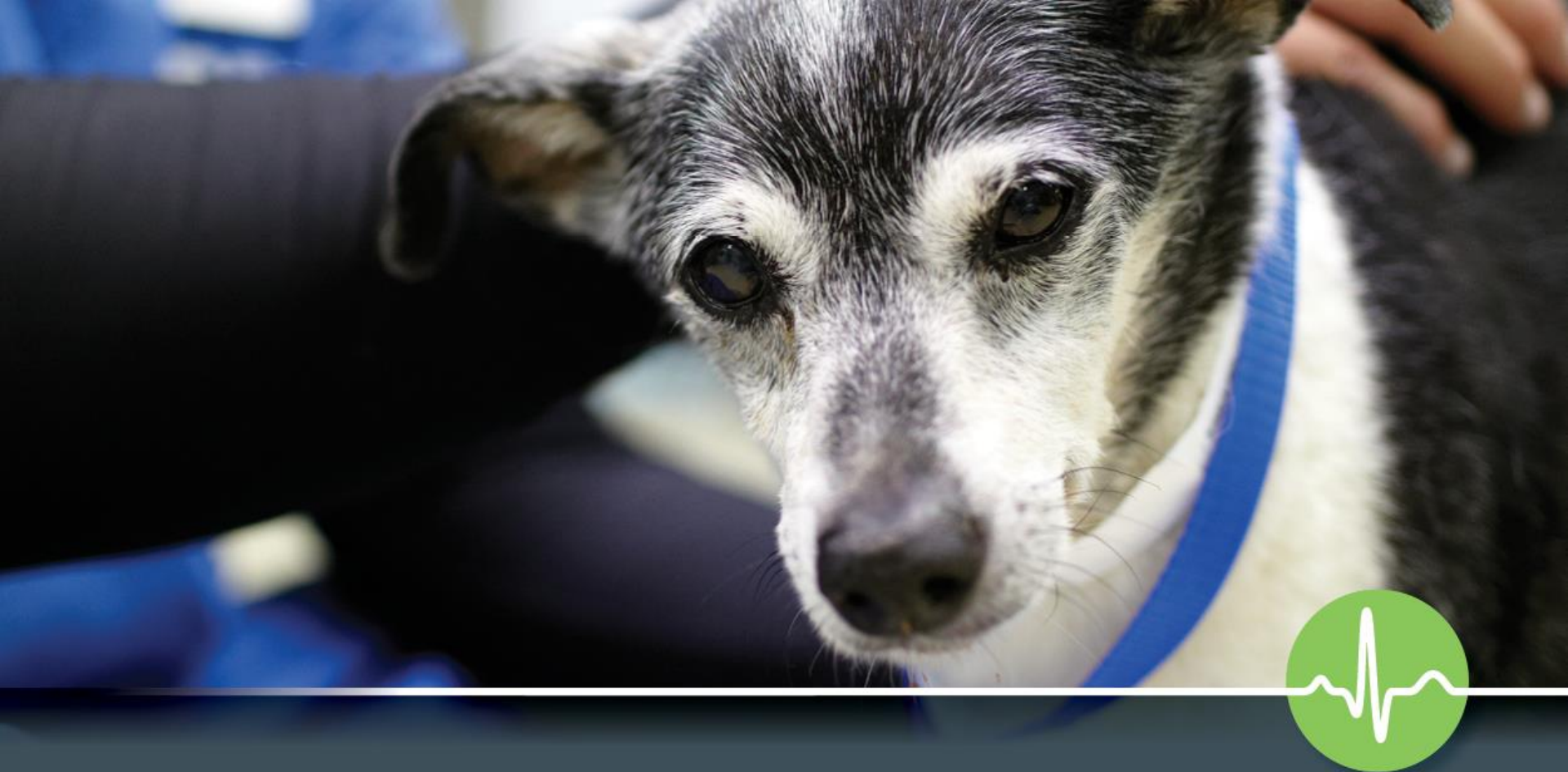




# SEIZURES VS. SYNCOPES







## CASE IV

## CASE IV



- 8 year old intact male Great Dane
- Generalized seizures started ~ 3-4 months ago
- Unremarkable blood work (CBC/Chem)
- Patient started on phenobarbital
  - continued having seizures
- Brain MRI was unremarkable
- Seizures became more frequent even though pheno dose was increased
- Presented to us for additional treatments for seizures
- Normal neurological and physical exam
- Phenobarbital level: 28  $\mu\text{g/mL}$



## CASE IV



- Review of rDVM's blood work
  - Unremarkable CBC
  - Biochemical profile unremarkable; however, BG consistently in lower end of normal range or mildly below normal
- Fasting BG = 40 mg/dL
- Insulin/glucose level
  - Consistent with insulinoma (high insulin with low BG)



# CASE IV

## Insulinoma

- Usually an islet cell carcinoma of the pancreas
- 60%-70% functional
- Hyperinsulinemia results in hypoglycemia by decreasing glucose production and increasing glucose utilization
- More commonly affects medium to large breed dogs
- Clinical signs are often episodic and caused by hypoglycemia and resultant neuroglycopenia



- Poor correlation between feeding and onset signs
- Seizures, collapse, and generalized weakness are the most common clinical signs
- Paraneoplastic peripheral polyneuropathy has been described in dogs
- Diagnostics
  - Abd u/s, CT scan, MRI, exploratory sx
- Treatment
  - Medical: prednisone, diazoxide, streptozotocin, etc.
  - Surgical



# SUMMARY

- Systematic approach in diagnosing and managing seizure patients
- Importance of diagnosing underlying cause
- Importance of history and neurological exam
- Minimum data base
- Realize many different presentations for seizures (esp. partial seizures)





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